

**REMARKS**

Claims 7-20 are pending in the application; each of the claims has been rejected.

Applicants request entry of the amendment filed October 9, 2002, which was refused entry in the Advisory Action dated October 21, 2002. Applicants note that the amendments to the claims presented herein assume entry of the amendment filed October 9, 2002, and the amendments to the claims herein are based on the claims as amended therein.

The claims are being amended to more clearly state that the series of selected biomolecules and selected detecting bodies are directly contacting the phosphor layer or the protective layer of the present invention. Support for the amendment may be found, for example, at page 16, line 22 through page 17, line 2, wherein it is stated that the arrayed molecules are fixed "on the surface of the protective layer" or "within the protective layer." Similar support is found at page 17, lines 3-14, wherein it is stated that the arrayed molecules are fixed "on the surface of the phosphor layer" or "within the phosphor layer."

The claims are also being amended to state that the series of selected biomolecules and selected detecting bodies are arrayed in a known configuration. Support for this amendment may be found in the specification, such as at page 10, beginning at line 15, where the arrangement of the biomolecules and detecting bodies is discussed. Further, at page 16, lines 15-21, where an example using cDNA is discussed, it is stated that the cDNA location has been previously stored, and was thus known prior to hybridization. It will be apparent from the specification that reference to a "known configuration" is with regard to the arrangement or location of the biomolecules and detecting bodies on the phosphor layer or the protective layer. The term

“configuration” does not refer to the three-dimensional characteristics of the individual biomolecules and detecting bodies (e.g., protein tertiary structure).

No new matter has been added. Entry of the amendment is earnestly solicited.

**I. Examiner Interview**

Applicants thank the Examiner for the helpful telephonic interview held on November 8, 2002. Therein, Applicants discussed with the Examiner the amendments to the claims being made herein. The Examiner indicated her agreement that the present specification provides support for the amendments to the claims included herewith, such that the arrays of biomolecules and detecting bodies are arranged “in a known configuration”, and that the biomolecules and detecting bodies are “affixed on or within” the phosphor layer and the protective layer. Therefore, no question of new matter should arise.

**II. Rejection of claims under 35 U.S.C. §102**

At paragraph 3 of the Office Action, claims 7, 8, 10 and 13-15 are rejected under 35 U.S.C. §102(b) as being anticipated by Shiraishi et al.

The Examiner asserts that the claims are drawn to a microarray comprising a stimutable phosphor sheet and multiple kinds of biomolecules arrayed and fixed on the phosphor sheet. The Examiner states that the claims are given their broadest reasonable interpretation consistent with the indefinite claim language, wherein it is unclear how the biomolecules are arrayed and fixed, and the specification wherein the microarray “has broad meanings embracing...a macro array.”

The Examiner then repeats the specific references to the claims first made in the Office Action dated August 14, 2001, using the numbering corresponding to the new claims.

In response, Applicants note that the Examiner states that because the biomolecules of Shiraishi et al. are resolved on a support medium (protective layer) wherein the support medium is adhered to the phosphor layer, the broadest interpretation of the claims would be anticipated by Shiraishi et al. However, Shiraishi et al. states that the support medium can be used for separation and identification of samples in the autoradiography. Shiraishi et al. also clearly states that the support medium is different from a protective layer on the phosphor sheet. Therefore, the teachings of Shiraishi et al., in which an electrophoretic gel is placed or mounted on a stimuable phosphor sheet, is clearly different from the present invention, in which biomolecules are affixed on or within a phosphor layer or a protective layer. This difference is clearly made in the claims wherein the words “affixed on or within” are used. At page 16, line 22 through page 17, line 2, of the specification it is stated that the arrayed molecules are fixed “on the surface of the protective layer” or “within the protective layer.” Similarly, at page 17, lines 3-14, of the specification it is stated that the arrayed molecules are fixed “on the surface of the phosphor layer” or “within the phosphor layer.” In contrast, the support medium of Shiraishi et al. is said to “resolve” biomolecules, and thus the biomolecules of Shiraishi et al. are not fixed on or within the phosphor layer. Instead, it is the support medium containing the biomolecules that is fixed on the phosphor layer. The words “affixed on or within” of the present invention do not encompass a support medium containing the biomolecules, that is in turn fixed on the phosphor layer.

In addition, Applicants note that the pending claims have been amended to clearly state that the series of selected biomolecules and the series of selected detecting bodies which are affixed on or within the phosphor layer or protective layer are arranged “in a known

configuration.” Thus, the identity and location of each biomolecule or detecting body is known prior to the use of the microarray (e.g., use of the microarray by hybridization with a labeled biomolecule).

In contrast, Shiraishi et al. provides no teaching or discussion of fixing the biomolecules resolved by gel electrophoresis in a known configuration. Nor would the identity and location of the biomolecules be known prior to hybridization with a labeled probe as Shiraishi et al. teaches hybridization prior to resolution in the support medium. Indeed, the skilled artisan would understand that the nature of the method discussed in Shiraishi et al. results in differential positioning of biomolecules depending on the characteristics of the biomolecules (e.g., size, charge, shape, etc.) and the gel matrix, and the conditions under which the biomolecules are resolved on the electrophoretic gel (e.g., buffer, current, etc.). Thus, Shiraishi et al. does not teach positioning of biomolecules in a known configuration, nor does the nature of the system taught in Shiraishi et al. allow one to position biomolecules at known positions.

In view of these comments, and the amendments to the claims, Applicants assert that Shiraishi et al. does not anticipate the claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

### **III. Rejection of claims under 35 U.S.C. §103**

A. At paragraph 5 of the Office Action, claims 11, 12 and 16-19 are rejected under 35 U.S.C. §103(a) as being unpatentable over Shiraishi et al. in view of Davis et al.

The Examiner repeats his rejection of the claims as being obvious over Shiraishi et al., in view of Davis et al., first set forth in the Office Action dated August 14, 2001, but using the numbering of the new claims. Briefly, the Examiner asserted that Shiraishi et al. teaches a

method for analyzing a biomolecule (claims 11 and 12) and a samples (claims 16 and 17), but does not teach labeling the fixed biomolecule by hybridization with a labeled biomolecule. However, the Examiner contends, labeling a biomolecule by hybridization with a labeled biomolecule was well-known in the art at the time of the invention as taught by Davis et al. Thus, the Examiner concludes, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the labeling of Shiraishi et al., using the teaching of Davis et al.

In response, Applicants assert that in view of the comments above, and the amendments to the claims, the disclosure of Shiraishi et al. does not render obvious the rejected claims. Indeed, Shiraishi et al. does not teach the fixation of biomolecules or detecting bodies on or within a phosphor layer or a protective layer.

Furthermore, Shiraishi et al. does not teach the arrangement of a series of selected biomolecules or a series of selected detecting bodies "in a known configuration."

Applicants further assert that the disclosure of Davis et al. does not teach or suggest fixation on or with the phosphor layer or protective layer, or an arrangement in a known configuration, and thus does not cure the deficiencies of Shiraishi et al.

Thus, the disclosure of Shiraishi et al., in view of Davis et al., does not make obvious the invention recited in the rejected claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

**B.** At paragraph 6 of the Office Action, claim 9 is rejected under 35 U.S.C. §103(a) as being unpatentable over Shiraishi et al. in view of Heller et al. (U.S. Patent No. 5,632,957).

The Examiner asserts that Shiraishi et al. teaches a microarray comprising a stimuable phosphor layer on a substrate and a protective layer on the phosphor layer, wherein the protective layer has affixed thereto an array of biomolecules wherein the protective layer comprises polyacrylamide and the biomolecules are affixed by electrophoretic resolution using “well-known” methods.

While the Examiner also states that Shiraishi et al. does not specifically teach the protective layer comprising poly-L-lysine, the use of polyacrylamide wherein the surface of the polyacrylamide is functionalized with poly-L-lysine is taught in Heller et al. (col. 18, lines 5-10). The Examiner concludes it would have been obvious to apply the surface modification taught by Heller et al. to the polyacrylamide surface of Shiraishi et al. to provide for covalent attachment of the biomolecules.

In response, Applicants assert that in view of the comments above, and the amendments to the claims, the disclosure of Shiraishi et al. does not render obvious the rejected claims. Indeed, Shiraishi et al. does not teach the fixation of biomolecules or detecting bodies on or within a phosphor layer or a protective layer, without a support medium containing them. Nor does Shiraishi et al. teach the arrangement of a series of selected biomolecules or a series of selected detecting bodies “in a known configuration.”

Applicants further assert that the disclosure of Heller et al. does not teach or suggest such fixation, or such an arrangement, and thus does not cure the deficiencies of Shiraishi et al.

Thus, the disclosure of Shiraishi et al., in view of Heller et al., does not make obvious the invention recited in the rejected claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

C. At paragraph 7 of the Office Action, claim 20 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Shiraishi et al., in view of Davis et al., as applied to claim 12 above, and further in view of Heller et al.

The Examiner states that Shiraishi et al. teaches a method for analyzing a biomolecule and a sample, as explained above. The Examiner further states that Heller et al. teaches the use of poly-L-lysine to functionalize the surface of the support medium (when it is polyacrylamide) and thereby provide for the covalent attachment of biomolecules, and that Davis et al. teaches the labeling of a biomolecule by hybridization with a labeled biomolecule was well-known in the art at the time of the invention.

In response, for each of the reasons recited above, Applicants assert that the disclosure of Shiraishi et al., in view of Davis et al. and Heller et al., does not render obvious the invention recited in the rejected claim. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

#### **IV. Conclusion**

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

SUPPLEMENTAL AMENDMENT  
U.S. Appln. No. 09/624,395

Q58690

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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**APPENDIX**

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE CLAIMS:**

**The claims are amended as follows:**

7. (Twice amended) A micro array, comprising a stimuable phosphor layer provided on a substrate, wherein affixed on or within said phosphor layer ~~is has affixed thereto~~ an array of a series of selected biomolecules in a known ~~predetermined~~ configuration.

8. (Twice amended) A micro array, comprising a stimuable phosphor layer provided on a substrate and a protective layer provided on said stimuable phosphor layer, wherein affixed on or within said protective layer ~~is has affixed thereto~~ an array of a series of selected biomolecules in a known ~~predetermined~~ configuration.

9. (Amended) The micro array of claim 8, wherein said protective layer is ~~biomolecules are affixed by bonding to a poly-L-lysine coated protective layer.~~

11. (Twice amended) A method for analyzing a biomolecule, comprising the steps of:

(i) preparing a micro array, wherein said micro array comprises a stimuable phosphor layer provided on a substrate, wherein affixed on or within said phosphor layer ~~is has affixed thereto~~ an array of a series of selected biomolecules in a known ~~predetermined~~ configuration,

(ii) contacting the micro array of step (i) with a labeled biomolecule, to cause the labeled biomolecule to be bound to one or more members of the series of selected biomolecules, wherein said labeled biomolecule is labeled with an energy generating substance,

(iii) exposing the resulting micro array of step (ii) to visible light to thereby induce the release of energy from phosphor molecules in the stimuable phosphor layer,

(iv) placing the micro array of step (iii) in a dark place to thereby cause the stimuable phosphor layer to store energy released from the energy generating substance,

(v) exposing the resulting micro array of step (iv) to stimulating rays which cause the stimuable phosphor layer to emit light in proportion to the amount of energy stored therein,

(vi) photoelectrically detecting the resulting emitted light from step (v) as a signal, so as to detect the one or more members of the series of selected biomolecules which are bound to the labeled molecule, and

(vii) determining the identity of the one or more members of the series of selected biomolecules bound to the labeled biomolecule by comparing the location of the detected signal in the micro array to the location of said one or more members of the series of selected biomolecules based on previously stored positional information.

12. (Twice amended) A method for analyzing a biomolecule, comprising the steps of:

(i) preparing a micro array, wherein said micro array comprises a stimuable phosphor layer provided on a substrate and a protective layer provided on said phosphor layer, wherein affixed on or within said protective layer ~~is has affixed thereto~~ an array of a series of selected biomolecules in a known predetermined configuration,

(ii) contacting the micro array of step (i) with a labeled biomolecule, to cause the labeled biomolecule to be bound to one or more members of the series of selected biomolecules, wherein said labeled biomolecule is labeled with an energy generating substance,

(iii) exposing the resulting micro array of step (ii) to visible light to thereby induce the release of energy from phosphor molecules in the stimuable phosphor layer,

(iv) placing the micro array of step (iii) in a dark place to thereby cause the stimuable phosphor layer to store energy released from the energy generating substance,

(v) exposing the resulting micro array of step (iv) to stimulating rays which cause the stimuable phosphor layer to emit light in proportion to the amount of energy stored therein,

(vi) photoelectrically detecting the resulting emitted light from step (v) as a signal, so as to detect the one or more members of the series of selected biomolecules which are bound to the labeled molecule, and

(vii) determining the identity of the one or more members of the series of selected biomolecules bound to the labeled biomolecule by comparing the location of the detected signal in the micro array to the location of said one or more members of the series of selected biomolecules based on previously stored positional information.

13. (Twice amended) A micro array, comprising a stimuable phosphor layer provided on a substrate, wherein affixed on or within said phosphor layer ~~is has affixed thereto~~ an array of a series of selected detecting bodies in a known ~~predetermined~~ configuration.

14. (Twice amended) A micro array, comprising a stimuable phosphor layer provided on a substrate and a protective layer provided on said stimuable phosphor layer, wherein affixed on or within said protective layer ~~is has affixed thereto~~ an array of a series of selected detecting bodies in a known ~~predetermined~~ configuration.

16. (Twice amended) A method for analyzing a sample, comprising the steps of:

(i) preparing a micro array, wherein said micro array comprises a stimuable phosphor layer provided on a substrate, wherein affixed on or within said phosphor layer is ~~has~~ ~~affixed thereto~~ an array of a series of selected detecting bodies in a known ~~predetermined~~ configuration,

(ii) contacting the micro array of step (i) with a sample, wherein said sample comprises a plurality of constituents which are labeled with an energy generating substance, to cause a constituent in said sample to be bound to one or more members of the series of selected detecting bodies,

(iii) exposing the resulting micro array from step (ii) to visible light to thereby induce the release of energy from phosphor molecules in the stimuable phosphor layer,

(iv) placing the micro array of step (iii) in a dark place to thereby cause the stimuable phosphor layer to store energy release from the energy generating substance,

(v) exposing the resulting micro array of step (iv) to stimulating rays which cause the stimuable phosphor layer to emit light in proportion to the amount of energy stored therein,

(vi) photoelectrically detecting the resulting emitted light from step (v) as a signal, so as to detect a labeled constituent of the sample which is bound to a detecting body, and

(vii) determining the identity of a labeled constituent of the sample by comparing the location of the detected signal in the micro array to the location of said one or more members of the selected detecting bodies based on previously stored positional information.

17. (Twice amended) A method for analyzing a sample, comprising the steps of:

(i) preparing a micro array, wherein said micro array comprises a stimuable phosphor layer provided on a substrate and a protective layer provided on said phosphor layer,

wherein affixed on or within said protective layer ~~is has affixed thereto~~ an array of a series of selected detecting bodies in a known ~~predetermined~~ configuration,

(ii) contacting the micro array of step (i) with a sample, wherein said sample comprises a plurality of constituents which are labeled with an energy generating substance, to cause a constituent in said sample to be bound to one or more members of the series of selected detecting bodies,

(iii) exposing the resulting micro array from step (ii) to visible light to thereby induce the release of energy from phosphor molecules in the stimuable phosphor layer,

(iv) placing the micro array of step (iii) in a dark place to thereby cause the stimuable phosphor layer to store energy release from the energy generating substance,

(v) exposing the resulting micro array of step (iv) to stimulating rays which cause the stimuable phosphor layer to emit light in proportion to the amount of energy stored therein,

(vi) photoelectrically detecting the resulting emitted light from step (v) as a signal, so as to detect a labeled constituent of the sample which is bound to a detecting body, and

(vii) determining the identity of a labeled constituent of the sample by comparing the location of the detected signal in the micro array to the location of said one or more members of the selected detecting bodies based on previously stored positional information.

20. (Amended) The method of claim 12, wherein said protective layer is ~~biomolecules are affixed by bonding to a poly-L-lysine coated~~ protective layer.